

1   **Supplemental Materials**

2

3   **Supplemental Figure Captions**

4   **Figure S1.**

5   **(A)** Gating scheme for fluorescent-activated cell sorting of convalescent SARS-CoV-1 donor.

6   Cells were initially stained with Ghost Red 780, CD14-APC-Cy7, CD3-FITC, CD19-BV711, and

7   IgG-PE-Cy5 along with a DNA-barcoded antigen screening library. To detect antigen-positive B

8   cells, cells were washed and treated with a streptavidin-PE secondary stain. Gates as drawn

9   are based on gates used during the sort, and percentages from the sort are listed.

10   **(B)** The categorization of processing of Cell Ranger identified cells after sequencing is shown.

11   **(C)** Genetic sequence characteristics of 15 antibody candidates. Percent identity is calculated at

12   the nucleotide level and CDRH3 and CDRL3 lengths and sequences are noted at the amino

13   acid level.

14   **(D)** ELISA binding data against coronavirus S antigens. HIV-specific antibody VRC01 was used

15   as a negative control and anti-SARS-CoV-1 mouse antibody 240CD was used as a positive

16   control (BEI Resources). ELISAs were performed in technical duplicates with at least two

17   biological duplicates.

18

19   **Figure S2.**

20   **(A)** Cross-reactive antibodies were tested for binding to SARS-CoV-2 S1 domain, SARS-CoV-2

21   S1 domain D614G, SARS-CoV-2 S2 domain, and SARS-CoV-2 S (HexaPro). Anti-HIV antibody

22   VRC01 is shown as a negative control and anti-SARS-CoV-1 antibody 240CD is shown as

23   positive control.

24   **(B)** S1-directed antibodies 46472-6 and 46472-12 were tested for binding against SARS-CoV-2

25   RBD, SARS-CoV-1 RBD, SARS-CoV-2 NTD, and SARS-CoV-2 S (HexaPro). Anti-HIV antibody

26 VRC01 is shown as a negative control and anti-SARS-CoV-1 antibody 240CD is shown as  
27 positive control.

28 (C) 46472-12 was tested for its ability to block ACE2 binding to SARS-CoV-2 S. Signal shown is  
29 anti-Flag tag detection of an ACE2-Flag tag protein construct.

30 (D) 46472-6 and 46472-12 were tested for binding to SARS-CoV-2 S (HexaPro) mutants,  
31 N165A and N709A, by ELISA.

32 (E) Mannose competition binding assays were performed to see if cross-reactive antibody  
33 binding to SARS-CoV-2 S could be modulated by mannose.

34

35 **Figure S3.**

36 (A) Antibodies were tested for neutralization in a SARS-CoV-1 and SARS-CoV-2 nano-  
37 luciferase neutralization assay.

38 (B) Antibodies were tested for neutralization in a SARS-CoV-2 RTCA assay.

39 (C) Cross-reactive coronavirus antibodies were tested for ability to mediate antibody-dependent  
40 cellular phagocytosis against SARS-CoV-2 S.

41 (D) Cross-reactive coronavirus antibodies were tested for ability to mediate antibody-dependent  
42 cellular phagocytosis against SARS-CoV-1 S coated on beads.

43 (E) Cross-reactive coronavirus antibodies were tested for ability to mediate antibody-dependent  
44 cellular trogocytosis against SARS-CoV-2 S coated on cells.

45 (F) Cross-reactive coronavirus antibodies were tested for ability to mediate antibody-dependent  
46 cellular trogocytosis against transfected cells displaying SARS-CoV-2 S

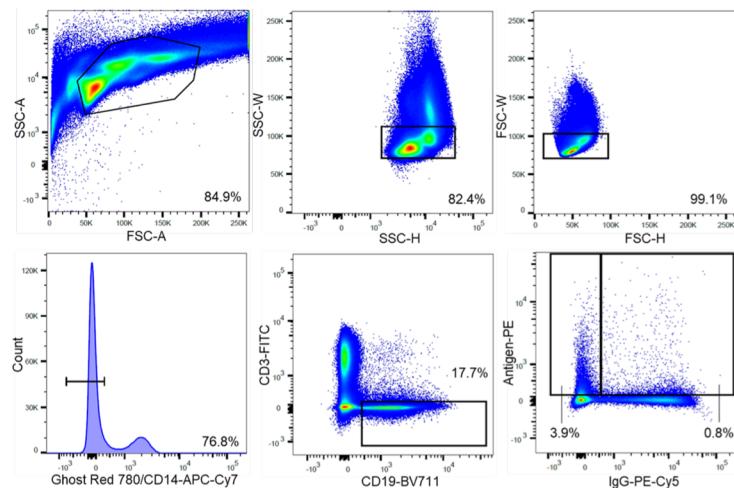
47 (G) Cross-reactive coronavirus antibodies were tested for ability to mediate antibody-dependent  
48 complement deposition against SARS-CoV-2 S.

49

50 **Figure S4.**

51 (A) For each antibody treatment group for the experiment utilizing  $1 \times 10^3$  PFU of SARS-CoV-2  
52 MA, a table showing the number of animals to survive per group, per day is shown. Body  
53 weights of each mouse in the four treatment groups were measured daily.  
54 (B) RT-qPCR quantification of lung viral titer is shown.  
55 (C) For each antibody treatment group for the experiment utilizing  $1 \times 10^4$  PFU of SARS-CoV-2  
56 MA, a table showing the number of animals to survive per group, per day is shown (survival  
57 curves shown in **Figure 4C**). 2/5, 4/5, 3/5, and 2/5 mice survived to day 4 for antibodies 46472-  
58 4, 46472-12, CR3022 and isotype control DENV-2D22 respectively. Body weights of each  
59 mouse in the four treatment groups in both experiments were measured daily.  
60 (D) RT-qPCR quantification of lung viral burden is shown.

A



## Supplemental Figure 1

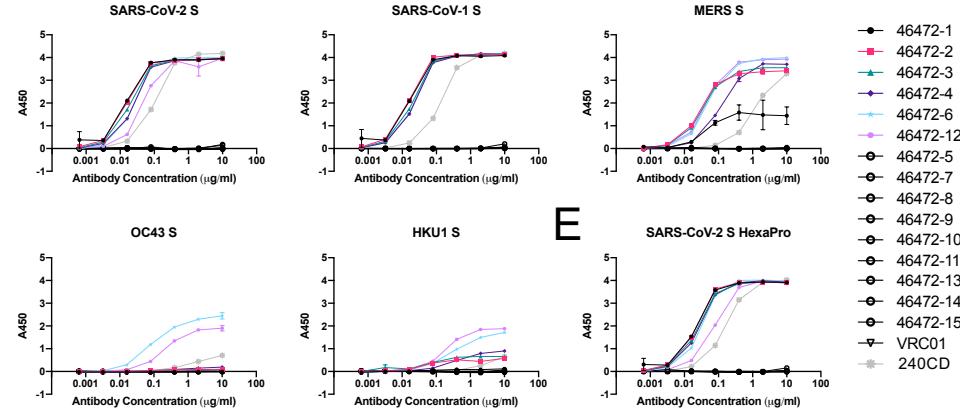
B

| 4647-2 Processing   |      |
|---|------|
| Unique Heavy Chain Barcodes   | 5113 |
| Unique Heavy Chain Barcodes With Functional Heavy Chains                  | 5072 |
| Unique Heavy Chain Barcodes Without Cells With Multiple Heavy Chains      | 4875 |
| Unique Light Chain Barcodes   | 7593 |
| Unique Light Chain Barcodes With Functional Light Chains                  | 7586 |
| Unique Light Chain Barcodes Without Cells With Multiple Light Chains      | 5914 |
| Unique Paired Heavy-Light Chain Barcodes                                  | 3813 |
| Overlapping Barcodes Between Paired Heavy-Light Chains and Antigen Counts | 2625 |

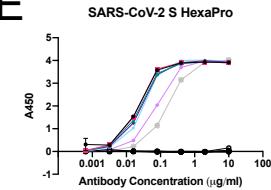
C

| Name     | VH gene  | VH % identity | CDRH3 length | VDJ junction            | VL gene  | VL % identity | CDRL3 length | VJ junction   |
|----------|----------|---------------|--------------|-------------------------|----------|---------------|--------------|---------------|
| 46472_1  | IGHV1-69 | 93.75         | 12           | AREVNYYSAFDD            | IGKV3-15 | 97.85         | 8            | QQYNFWWT      |
| 46472_2  | IGHV5-10 | 94.10         | 20           | AAAGPTGYDLLTGQYFPFYFN   | IGLV6-57 | 95.19         | 9            | QSYHGSDVV     |
| 46472_3  | IGHV3-30 | 94.79         | 14           | ARDRSATYYGPFDY          | IGLV3-19 | 94.98         | 12           | NSRDNSGNHPVI  |
| 46472_4  | IGHV3-23 | 90.97         | 19           | AKDLLSHSGTYSAGSTFDY     | IGKV1-39 | 94.98         | 8            | QESYSTNT      |
| 46472_5  | IGHV4-39 | 84.19         | 9            | ARLDYSKQT               | IGKV2-28 | 96.26         | 9            | MQALQTPLT     |
| 46472_6  | IGHV4-39 | 90.72         | 24           | ARRPQYLLSMTTGRHHDFVMDV  | IGKV4-1  | 97.31         | 9            | QQYNNTPRT     |
| 46472_7  | IGHV3-64 | 92.36         | 11           | VKEDTPLVFDs             | IGKV1-5  | 93.19         | 8            | QQYDSYST      |
| 46472_8  | IGHV3-53 | 84.91         | 12           | ALGRKDYGDDYR            | IGKV3-20 | 89.01         | 11           | QQYAPSPPWYI   |
| 46472_9  | IGHV4-61 | 95.53         | 15           | ASLPTYGSGRWGIDS         | IGKV1-12 | 96.42         | 9            | QQGNSFPPLT    |
| 46472_10 | IGHV3-53 | 92.63         | 16           | AGFLPVYNNNGWSYFDS       | IGLV1-44 | 95.09         | 11           | AVVDDSLNGPV   |
| 46472_11 | IGHV3-23 | 87.15         | 13           | VKMRTAVVGVTPL           | IGKV1-6  | 95.34         | 9            | LQDNYNLFS     |
| 46472_12 | IGHV1-8  | 92.01         | 20           | ARDRVERTGNVGFYYAMDV     | IGKV1-39 | 95.34         | 10           | QQTYSSPSYT    |
| 46472_13 | IGHV3-7  | 90.97         | 15           | ARVTIVSSFTNRDP          | IGKV1-9  | 90.32         | 5            | QHRVT         |
| 46472_14 | IGHV3-53 | 82.81         | 6            | VRGRTY                  | IGKV3-15 | 92.47         | 9            | QQYNRNLWLT    |
| 46472_15 | IGHV7-4  | 97.57         | 23           | ARDFDLVVPSATYPPFYHHGMDV | IGLV3-19 | 97.49         | 13           | NSRDSSGDQTFYV |

D

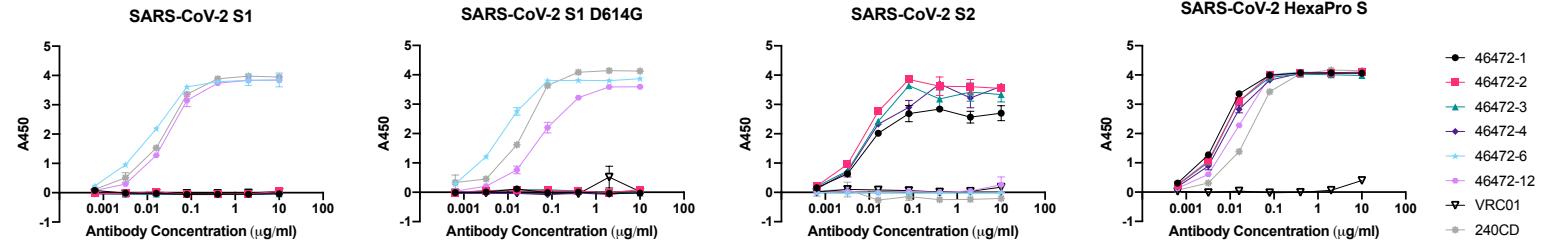


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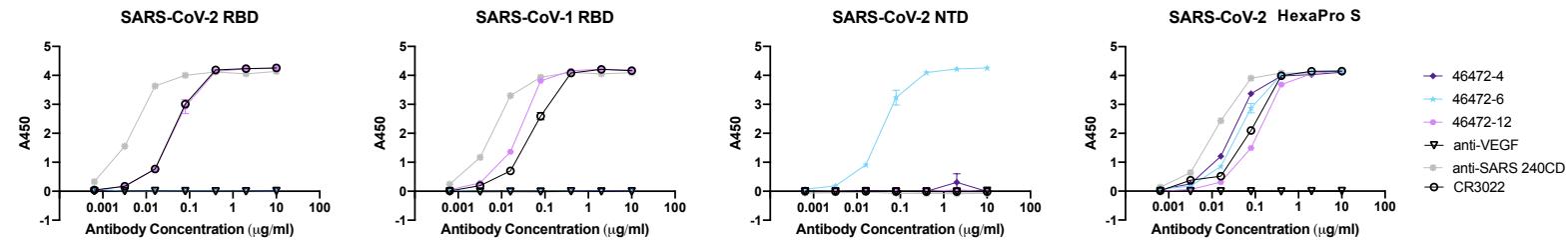


## Supplemental Figure 2

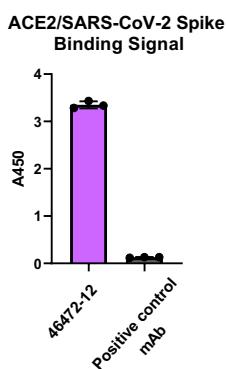
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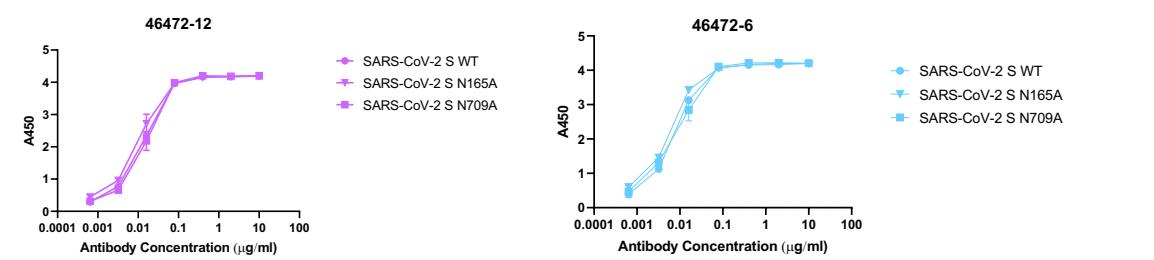
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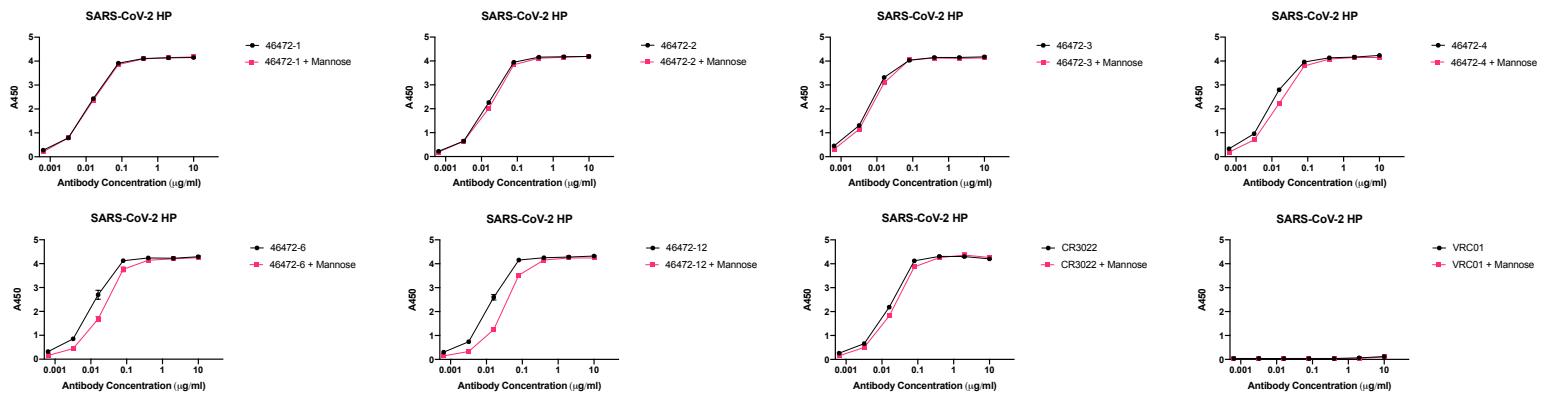
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D

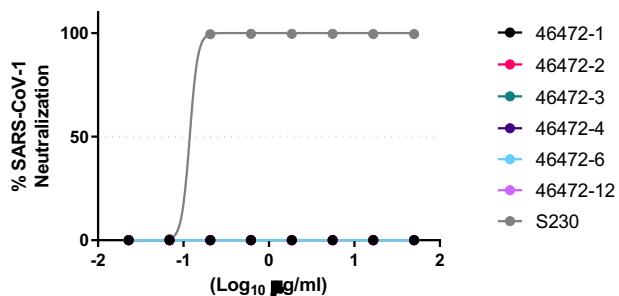


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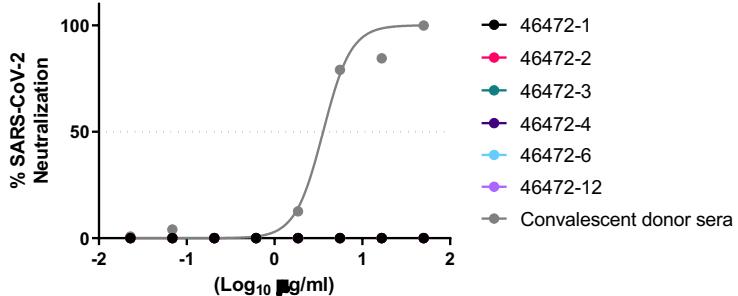
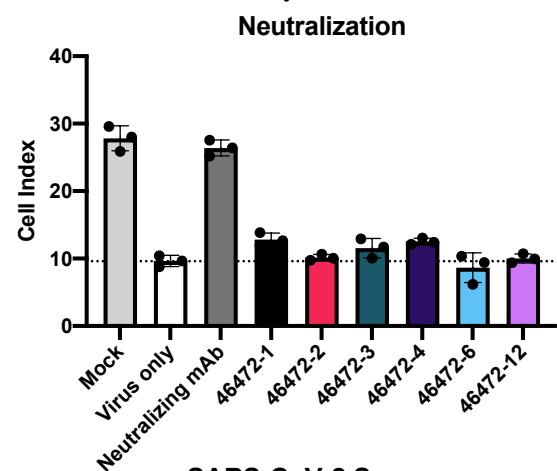


# Supplemental Figure 3

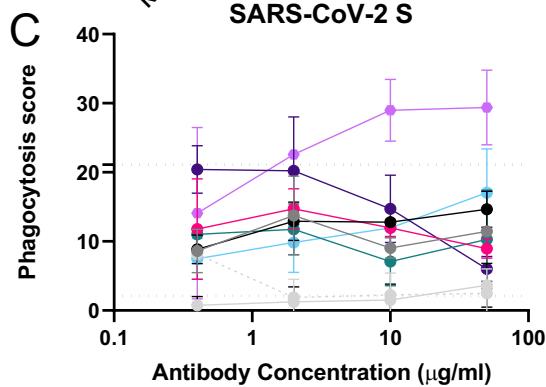
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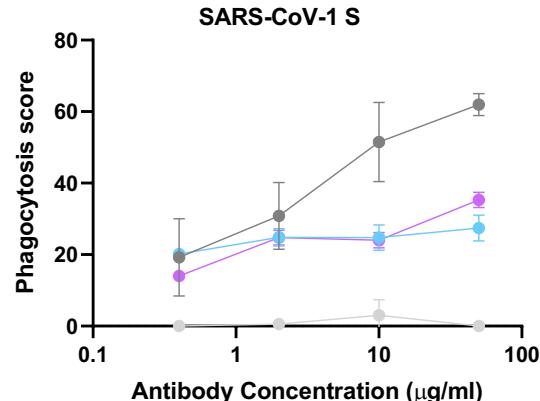
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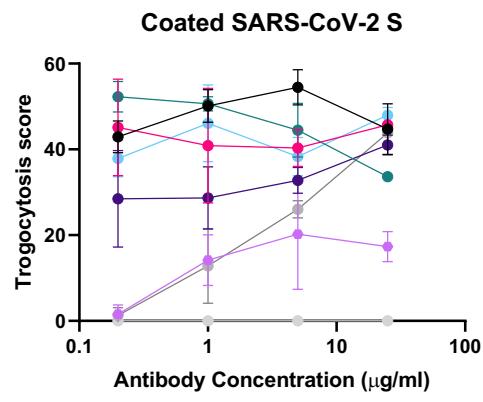
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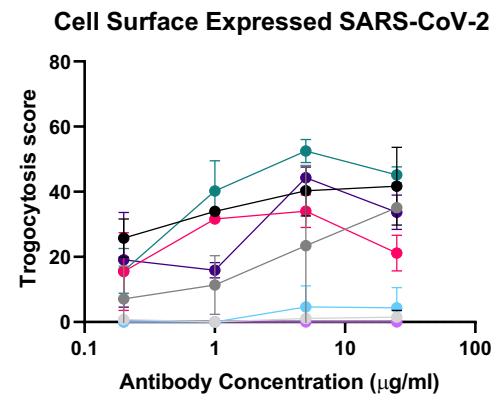
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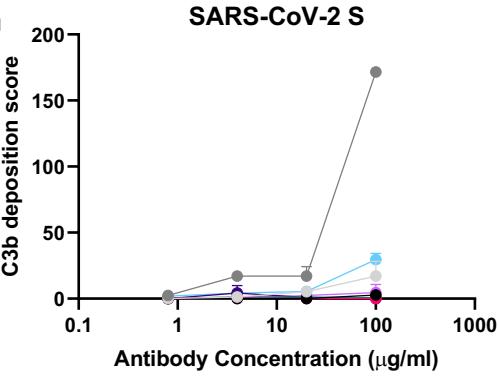
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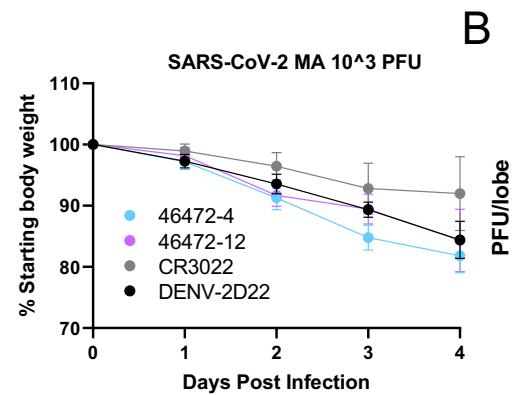


- CR3022
- Palivizumab
- 46472-1
- 46472-2
- 46472-3
- 46472-4
- 46472-6
- 46472-12

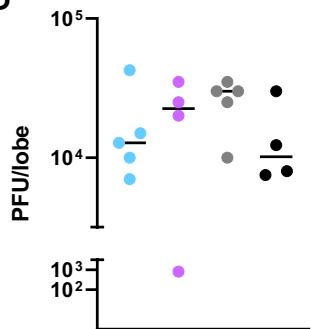
## Supplemental Figure 4

A

| Antibody  | Animal Survival, Days Post Infection |     |     |     |     |
|-----------|--------------------------------------|-----|-----|-----|-----|
|           | 0                                    | 1   | 2   | 3   | 4   |
| 46472-12  | 4/4                                  | 4/4 | 4/4 | 4/4 | 4/4 |
| 46472-4   | 5/5                                  | 5/5 | 5/5 | 5/5 | 5/5 |
| CR3022    | 5/5                                  | 5/5 | 5/5 | 5/5 | 5/5 |
| DENV-2D22 | 5/5                                  | 5/5 | 5/5 | 5/5 | 4/5 |

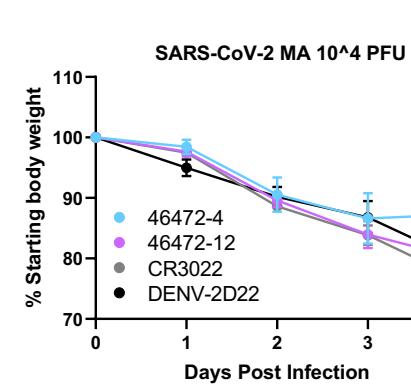


B



C

| Antibody  | Animal Survival, Days Post Infection |     |     |     |     |
|-----------|--------------------------------------|-----|-----|-----|-----|
|           | 0                                    | 1   | 2   | 3   | 4   |
| 46472-12  | 5/5                                  | 5/5 | 5/5 | 5/5 | 4/5 |
| 46472-4   | 5/5                                  | 5/5 | 5/5 | 4/5 | 2/5 |
| CR3022    | 5/5                                  | 5/5 | 5/5 | 4/5 | 3/5 |
| DENV-2D22 | 5/5                                  | 5/5 | 5/5 | 5/5 | 2/5 |



D

